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PHYSICIAN CONNECT

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Physician Connect" which contains latest and interesting news.

This issue contains:

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A comprehensive review and meta-analysis of 1.4 million diabetic patients found a link between hypoglycemia and dementia

Hypoglycemia is a condition in which the patient's blood glucose level is low, placing them at risk of damage. Severe hypoglycemia is common in people with type 1 diabetes, with an annual incidence ranging from 3.3 percent to 13.5 percent. In diabetic patients, hypoglycemia produces physical and psychological morbidity. Symptomatic hypoglycemia is both a source of alarm and a source of distraction. It has the potential to impair judgement, daily tasks such as driving, and behaviour. Hypoglycemia can cause seizures and loss of consciousness in more severe situations. Transient neurological deficiencies can occur, and irreversible neurological damage can occur in rare cases.[1] Insulin is involved in both glucose-driven mitochondrial bioenergetics and signal transduction pathways in neurons, which are required for neural progenitor/stem cell proliferation, migration, differentiation, neuronal outgrowth, and plasticity. Synapse malfunction and acetylcholine deficit are caused by abnormal insulin production, which has been linked to the aetiology of neurodegenerative disorders.[2] Diabetes mellitus (DM) is well-known as a dementia risk factor. However, it's uncertain if hypoglycemia incidents play a role in dementia risk. As a result, the goal of this study was to conduct a comprehensive evaluation of the information on the risk of dementia in diabetic individuals with prior hypoglycemia crises.[3]

Until November 15, 2021, the PubMed, Embase, ScienceDirect, CENTRAL, and Google Scholar databases were searched for cohort studies estimating the risk of dementia in diabetic patients based on prior hypoglycemia incidents. A random-effects model was used to pool the adjusted data.

A total of 1,407,643 patients were involved in ten research. Hypoglycemia episodes were related with a statistically significant increase in the risk of dementia in DM patients as compared to those who did not have hypoglycemic episodes (HR: 1.44 95 percent CI: 1.26, 1.65 I 2= 89 percent p <0.00001), according to a pooled analysis of all ten investigations. Excluding any study that had no effect on the results. Subgroup analysis based on the study population, study type, glycated haemoglobin adjustment, gender, and the frequency of hypoglycemic episodes yielded comparable results. In both retrospective and prospective investigations, hypoglycemia was found to have a consistent effect in increasing the risk of dementia. According to subgroup analysis depending on study site, the link between hypoglycemia and dementia was found in both Asian and Western populations. The analysis also divided between studies that included only type 2 diabetes and trials that included both types of diabetes.

Variable	Groups	No of studies	Hazard ratio
Study population	Asian	3	1.21 95% 01:1.02, .43 I = 67% p =0.03
	Western	7	1.5595% CI:1.31, 1.82 12 = 87% p<0.00001
Study type	Prospective cohort	4	1.8495% 1 = 66% p =0.005
	Retrospective cohort	6	1.3795% CI:1.18, 1.59 I = 93% p <0.0001
Type of DM	Only type DM	7	1.3295% 1.46 P = 71% p <0.00001
	Both types of DM	2	1.7395% 1:1.62, 1.85 p = 0% p <0.00001
Adjustment for glycated hemoglobin	Yes	7	1.5095% C1:1.27,1.77 P = 86% p <0.00001
	No	3	1.35 95% 01:07, 1.71 P = 86% p =0.01
Gender	Male	2	1.1895% CI:1.05, 1.33 P = 0% p 0.006
	Female	2	1.3095% 1.19, 1.41 p = 0% p <0.00001
No of hypoglycemic episodes	1 episode	3	1.2195% CI:1.11, 1.32 F = 0% p <0.0001
	2 episodes	3	1.63 95% 1.10, 1.43 1 = 84% p =0.02

Sub-group analysis association between hypoglycemic episodes and risk of dementia

This 1.4 million patient meta-analysis shows substantial evidence for the link between hypoglycemia incidents and dementia risk in diabetes individuals. This quantitative research revealed that patients who experience hypoglycemia episodes had a 44 percent higher risk of dementia than those who do not.[3] The Lee AK et al study found a substantial relationship between severe hypoglycemia and poor cognitive results, indicating that appropriate diabetes therapies for high-risk older persons should be discussed.[4]

According to observational studies, diabetic patients who have had prior hypoglycemia crises had a 44 percent higher risk of dementia. The lower level of plasma glucose, which considerably increases the burden of dementia, should be the focus of future research. Studies should also look into whether the frequency of hypoglycemia incidents affects the risk of dementia.

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Autoantibodies against apoB100 p210 have been linked to a decreased risk of atrial fibrillation in women.

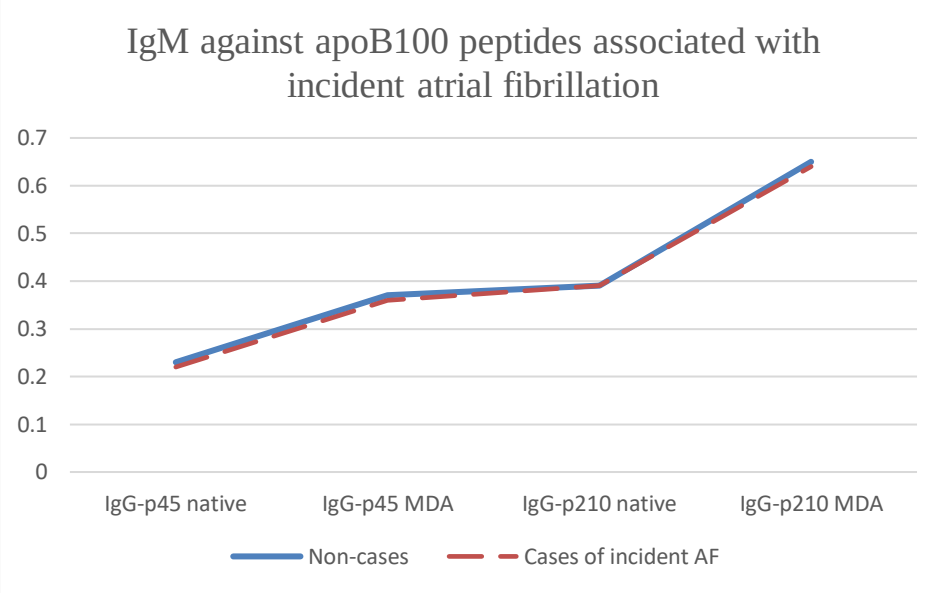
With an estimated global frequency of 34 million, atrial fibrillation (AF) is the most frequent kind of arrhythmia that causes hemodynamic problems, thrombotic strokes, heart failure, and increased mortality.[1] During the postoperative period of cardiovascular surgery, arrhythmias cause problems in 15% to 40% of patients. The prevalence of postoperative arrhythmias rises with age, from 18 percent in patients over 60 to 50 percent in octogenarians. These arrhythmias have a complicated aetiology that involves a pre-existing and perioperative substrate.[2] Patients with AF have higher levels of oxidised low-density lipoprotein (LDL), which is thought to be one of the chemicals that causes inflammation. Atherosclerosis is connected to autoantibodies against oxidised LDL and apolipoprotein B100, the protein component of LDL. However, it is unknown if these autoantibodies are linked to the development of AF. In a large population-based cohort, researchers looked at autoantibodies against oxidised apolipoprotein B100 peptides and the incidence of AF.[3]

In 5169 people from the Malmö Diet and Cancer cohort, IgM and IgG against native and aldehydemodified apoB100 peptides 210 (p210) and 45 were measured using an enzyme-linked immunosorbent test (ELISA). Histograms, skewness, and kurtosis measurements were used to examine the distributions of continuous variables. The two-tailed Student's t-test or Mann–Whitney U-test for continuous data and 2 or Fisher's exact test for categorical data were used to compare non-cases and cases.

During a follow-up period of 21.3 years, 769 incident AF instances were recorded. Individuals with high levels of IgM against native p210 had a decreased probability of getting AF at baseline; however, the link did not hold after age and sex were taken into account. IgM levels against native p210 were greater in women than in men (0.70 0.22 AU vs. 0.63 0.21 AU, p 0.001). After adjusting for risk factors and comorbidities, the relationship between IgM against native p210 and AF was significantly different between sexes (p for interaction = 0.024), with females with high IgM against p210 having a lower risk of AF (hazard ratio [95 percent confidence interval] 4th versus 1st quartile: 0.67 [0.49–0.91]; p = 0.01).

	Non-cases (n 4400)	Cases of incident AF (n 769)
IgM-p45 native	0.30 (0.13-0.58)	0.30 (0.14-0.54)
IgM-p45 MDA	0.43 (0.26-0.68)	0.40 (0.24-0.64)*
IgM-p210 native	0.67 (0.52-0.82)	0.64 (0.49-0.80)*
IgM-p210 MDA	0.75 (0.61-0.88)	0.73(0.57-0.86)
IgG-p45 native	0.23 (0.10-0.47)	0.22(0.095-0.48)
IgG-p45 MDA	0.37 (0.24-0.56)	0.36 (0.23-0.57)
IgG-p210 native	0.39 (0.29-0.53)	0.39 (0.27-0.53)
IgG-p210 MDA	0.65 (0.49-0.83)	0.64 (0.48-0.82)

Levels of autoantibodies against apoB100 peptide 45 and peptide 210 in non-cases and cases of incident atrial



In this investigation, autoantibodies against native and MDAmodified apolipoprotein B100 p45 and p210, as well as the risk of AF, were studied in a prospective population-based study with over 20 years of follow-up. Individuals with high levels of IgM against native p210, MDA-p210, and MDA-p45 had a decreased risk of AF than those with low autoantibody levels at baseline. When controlling for AF-related risk variables and comorbidities, however, these relationships were removed. Females were shown to have higher levels of IgM against p210 than males. Furthermore, IgM against native p210 was linked to a lower risk of AF in females but not in males, indicating a gender difference.[3] In atherosclerotic disease, oxidised LDL is thought to play a key role in arterial wall inflammation, and antibodies against oxidised LDL appear to protect against the illness.[4] A p210 monoclonal antibody binds aldehyde-modified LDL but not native LDL, showing that p210 is accessible during LDL oxidation. As a result, it's very likely that at least some of the autoantibodies measured in the current study recognise aldehyde-modified LDL. It's possible that p210 IgM, by binding to oxidised LDL in the atrial tissue, plays a protective role in AF.[5]

In conclusion, the study found that high levels of IgM against apoB100 p210 are related with a lower chance of developing AF in women, indicating that humoral autoimmunity may play a role in the development of AF.

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Effects of Sleep Extension in Real-Life Settings on Objectively Assessed Energy Intake in Overweight Adults

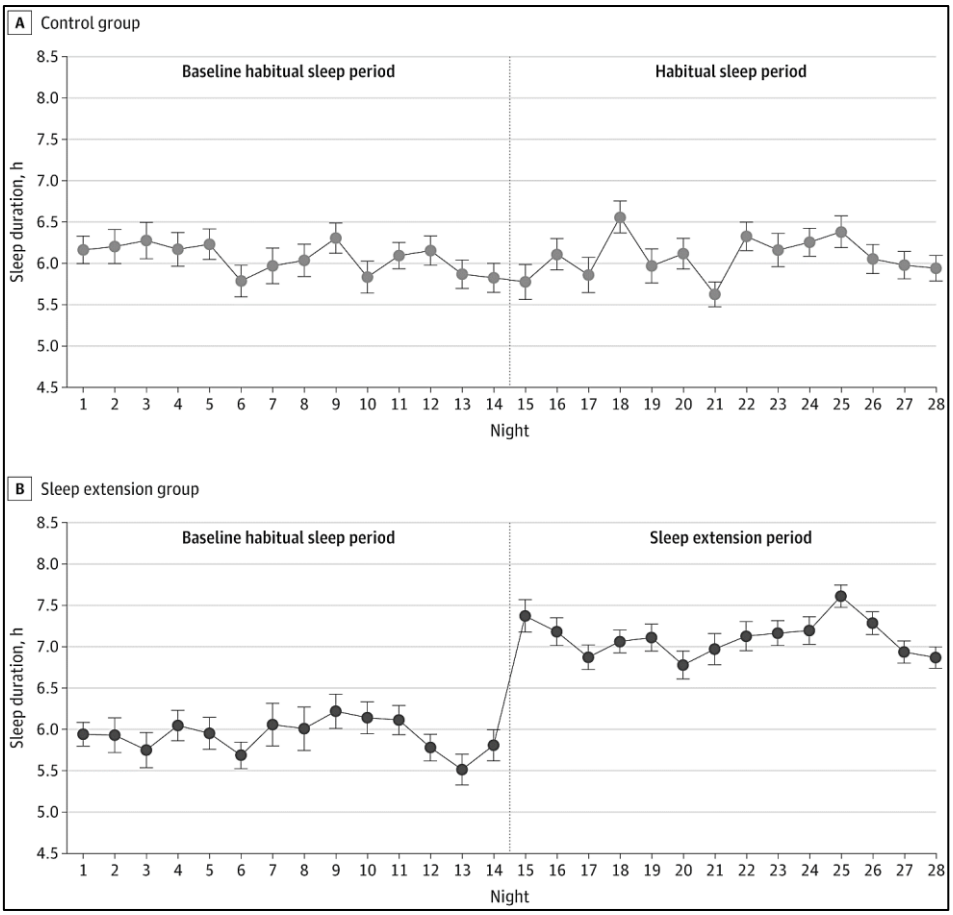
Obesity is a worldwide problem that affects children, adolescents, and adults. According to the World Health Organization (WHO), 36.9% of male adults and 38.0 percent of female adults worldwide are fat or overweight. In addition, there are around 500 million obese people and 2 billion overweight people in the world. Obesity has been linked to a variety of health issues, including metabolic syndrome, insulin resistance (IR), type 2 diabetes mellitus (T2DM), cardiovascular disease, hypertension, dyslipidemia, and cancer.[1] One of the most important factors in optimal functioning and wellbeing is adequate sleep. The immune system, metabolism, and mental health are all affected by lack of sleep. Adults should sleep for about 7 hours every night, according to the American Academy of Sleep Medicine (AASM) and the Sleep Research Society (SRS), because lower sleep duration has been linked to negative health outcomes. Short and lengthy sleep durations have both been linked to an increased risk of mortality, type 2 diabetes, CVD, stroke, CHD, and obesity.[2]

In most cases, sleep deprivation was severe, and calorie intake was estimated based on a single or a few meals. Multiple interacting factors can influence energy intake or expenditure, as well as weight, in a real-life scenario where participants go about their everyday activities. It is uncertain whether and to what extent a sleep duration-increasing intervention in a real-life environment affects energy balance and body weight. The aim of this study was to see how a sleep extension intervention affected objectively measured calorie intake, energy expenditure, and body weight in real-life conditions among overweight adults who were used to sleeping less.[3]

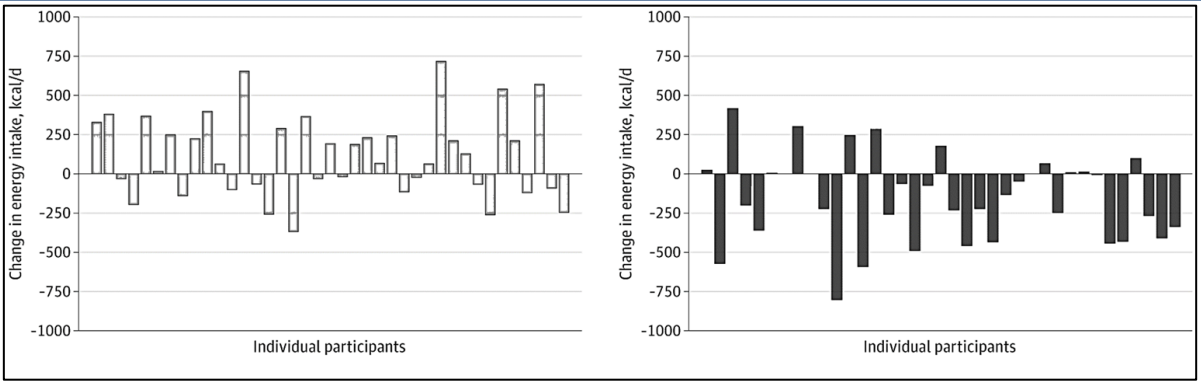
From November 1, 2014, until October 30, 2020, a single-center, randomised clinical trial was undertaken. Adults aged 21 to 40 years old with a body mass index (BMI) of 25.0 to 29.9 and an average sleep duration of fewer than 6.5 hours per night were included in the study. The data was evaluated with the intent-to-treat principle in mind. Participants were randomised to either a personalised sleep hygiene counselling session aimed at extending their bedtime to 8.5 hours (sleep extension group) or to continue their habitual sleep pattern (control group) after a 2-week habitual sleep period at baseline (control group). All of the participants were told to go about their normal routines at home without any kind of diet or physical exercise.

The results were examined from 80 randomised participants (mean [SD] age, 29.8 [5.1] years; 41 men [51.3 percent]). In the sleep extension group vs. the control group, sleep duration

increased by about 1.2 hours per night (95 percent CI, 1.0 to 1.4 hours; P.001). When compared to the control group, the sleep extension group consumed significantly less energy (270 kcal/d; 95 percent CI, 393 to 147 kcal/d; P.001). The change in sleep duration was inversely related to the change in energy intake (r = 0.41; 95 percent confidence interval, 0.59 to 0.20; P.001). There was no significant treatment effect on overall energy expenditure, however the sleep extension group lost weight compared to the control group. Sleep extension reduced calorie intake and resulted in a negative energy balance in real-life conditions in this RCT of overweight adults who had previously limited their sleep length.



Mean Nightly Sleep Duration by Wrist Actigraphy in Control and Sleep Extension Groups



Change from Baseline in Sleep Duration and Energy Intake in Individual Participants

This study is the first to show that prolonging sleep to a healthy duration has a positive impact on objectively measured energy intake and body weight in participants who stayed in their homes. Modest modifications in energy intake or expenditure are increasingly being suggested as feasible therapies for obesity reversal. The study revealed a 1.2-hour increase in objective sleep duration among participants who slept fewer than 6.5 hours per night on average in this RCT. In the real-life scenario, the change in sleep duration from baseline varied amongst subjects and from night to night. In real-life situations, Pizinger TM et colleagues tried bedtime extension in chronic short sleepers but found varying improvements on sleep, most likely due to a lack of a personalised approach or suitable blinding.[4]

Short-term sleep extension lowered objectively assessed energy intake and resulted in a negative energy balance in real-life circumstances among overweight people who had previously limited their sleep length, according to this RCT. The findings underscored the necessity of increasing public awareness about the benefits of adequate sleep duration for healthy weight maintenance and developing and maintaining adequate sleep duration as a public health objective for obesity prevention.

Reference:

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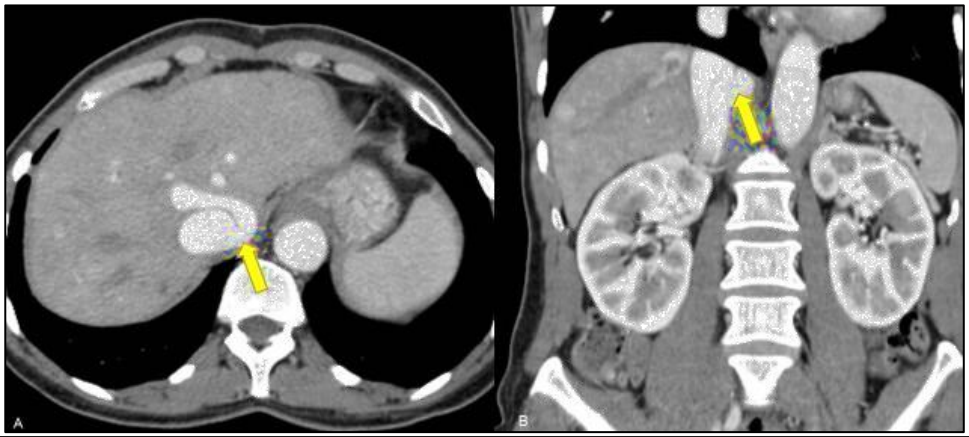
A Rare Cause of Hepatic Encephalopathy in Adults: Type II Abernethy Malformation

Abernethy malformation (AM), commonly known as congenital extrahepatic portosystemic shunts, is an uncommon vascular aberration of the portal venous system (CPSS). With no intrahepatic portal vein, an end-to-side porto-caval shunt exists in type I Abernethy malformation, and the portal vein bypasses the liver and empties straight into the IVC. A side-to-side porto-caval shunt is present in type II Abernethy malformation, and intrahepatic portal venous is preserved but hypoplastic. Severe complications from Abernethy malformation include liver tumours, hepatic encephalopathy, hepatopulmonary syndrome, and pulmonary hypertension.[1]

The case of a 50-year-old lady with hepatic encephalopathy but no liver impairment was given in the study.

A 52-year-old woman was sent to an internal medicine specialist after experiencing recurring episodes of attention impairment and confusion during the previous two years (with varying degrees of severity). She'd been to the emergency room (ED) twice before for these occurrences. She was diagnosed with metabolic encephalopathy at the second visit and was discharged following lactulose and hydration therapy. She had a history of venous insufficiency in her legs. She didn't take any long-term medications and denied ever abusing alcohol or drugs. She appeared to be aware and oriented, capable of following complex commands, and free of specific neurological abnormalities.

Laboratory testing was redone during the consultation, revealing ammonia levels that were lower than previously reported but still elevated when compared to normal norms (64 g/dl). In addition, serological tests for ceruloplasmin, hepatitis viruses, and immunological markers came back negative. A contrast-enhanced computed tomography (CT) scan of the abdomen revealed a 13-mm portocaval shunt from the left portal branch, indicating type II Abernethy malformation. The ultrasound elastography of the liver revealed normal stiffness. As a result, the patient's symptoms were



Axial (A) and coronal (B) CT images, in portal venous phase, showing a latero-lateral portocaval shunt of the left portal branch

attributed to portosystemic shunt-induced hepatic encephalopathy. The patient started taking lactulose and rifaximin (a non-absorbable antibiotic), which helped him feel better and reduced his encephalopathy episodes, but not completely. As a result, she was referred to vascular surgery for a shunt closure examination, and she is currently awaiting surgery.[2]

Abernethy malformation is an uncommon disorder in which portomesenteric blood drains into a systemic vein via a partial or complete shunt, bypassing the liver. On the basis of the shunt pattern between the portal vein and a systemic vein, it is divided into two categories. Abernethy malformation is linked to a variety of congenital and acquired problems. To interpret imaging findings, a thorough understanding of anatomy and embryology is required. The anatomy of the shunt can be delineated and associated abnormalities can be evaluated using computed tomography and magnetic resonance angiography.[3] There is currently a lack of therapeutic expertise with Abernethy deformity. Type I AM patients typically require liver transplantation, although type II AM patients may benefit from shunt closure, which can be done surgically or

percutaneously. To avoid post-procedure portal hypertension, it is vital to maintain enough portal vein capacity and normal portal pressure before shunt closure. The intrahepatic portal system should be assessed using angiography and the shunt-occlusion test in this regard.[4]

Abernethy malformation, despite being a rare cause of hepatic encephalopathy, should be examined in patients with unexplained hyperammonaemia. The patient in the cited case had been experiencing symptoms for two years and had been to the emergency room twice without the disease being diagnosed. Because Abernethy malformation is possibly reversible, it is critical to promote awareness of it. Furthermore, early detection and treatment may enhance the prognosis.

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